# IDDESIA . IEEDD2

# FIGURE 1

IJ	<u>ATG</u> TCAGTGGGAGCC <u>ATG</u> AAGAAGGGAGTGGGGAGGGCAGTTGGGCTTGGAGGCGGCAGC	09
61	GGCTGCCAGGCTACGGAGGAAGACCCCCTTCCCGACTGCGGGGCTTGCGCTCCGGGACAA	120
121	GGTGGCAGGCGCTGCCGCAGCCTGCGTGGGTGGAGGGGGAGCTCAGCTCGGTTG	180
181	TGGGAGCAGCGCCACTGGCTGGATGGACCTGGAAGCCTCGCTGCTGCCCACTGGT	240
241	CCCAATGCCAGCAACACCTCTGATGGCCCCGATAACCTCACTTCAGCAGGATCACCTCCT	300
301	CGCACGGGGAGCATCTCCTACATCATCATCATGCCTTCGGTGTTCGGCACCATCTGC	360
361	CTCCTGGGCATCATCGGGAACTCCACGGTCATCTTCGCGGTCGTGAAGAAGTCCAAGCTG	420
421	CACTGGTGCAACAACGTCCCCGACATCTTCATCATCAACCTCTCGGTAGTAGATCTCCTC	480
481	TTTCTCCTGGGCATGCCCTTCATGATCCACCAGCTCATGGGCAATGGGGTGTGGGCACTTT	540
541	GGGGAGACCATGTGCACCCTCATCACGGCCATGGATGCCAATAGTCAGTTCACCAGCACC	009
601	TACATCCTGACCGCCATGGCCATTGACCGCTACCTGGCCACTGTCCACCCCATCTCTTCC	099
661	ACGAAGTTCCGGAAGCCCTCTGTGGCCACCCTGGTGATCTGCCTCCTGTGGGCCCTCTCTC	720
721	TTCATCAGCATCACCCCTGTGTGGCTGTATGCCAGACTCCATCCCCTTCCCAGGAGGTGCA	780
781	GTGGGCTGCGGCATACGCCTGCCCAACCCAGACACTGACCTCTACTGGTTCACCCTGTAC	840
841	CAGTTTTTCCTGGCCTTTGCCCTGCCTTTTGTGGTCATCACAGCCGCATACGTGAGGATC	900
901	CTGCAGCGCATGACGTCCTCAGTGGCCCCCGCCTCCCAGCGCAGCATCCGGCTGCGGACA	096
961	AAGAGGGTGACCCGCACAGCCATCGCCATCTGTCTGGTCTTTGTGTGTG	1020
.021	TACTATGTGCTACAGCTGACCCAGTTGTCCATCAGCCGCCCGACCCTCACCTTTGTCTAC	1080
.081	TTATACAATGCGGCCATCAGCTTGGGCTATGCCAACAGCTGCCTCAACCCCTTTGTGTAC	1140
141	ATCGTGCTCTGTGAGACGTTCCGCAAACGCTTGGTCCTGTCGGTGAAGCCTGCAGCCCAG	1200
201	GGGCAGCTTCGCGCTGTCAGCAACGCTCAGACGGCTGACGAGGAGGAGGACAGAAAGCAAA	1260
.261	GGCACCIGA	1269

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41	G	G	R	R	W	R	L	P	Q	P	A	W	V	Ε	G	s	s	Α	R	L	60
61	W	E	Q	Α	Т	G	Т	G	W	М	D	L	E	Α	s	L	L	P	Т	G	80
81	P	N	A	s	N	T	s	D	G	P	D	N	L	Т	s	A	G	s	P	P.	100
101	R	Т		s	I	s	Y	I	N	I	Ι	M	Р	s	v	F	G	T	I	С	120
121	L	L	_	I	Ι	G	N	s	Т	v	Ι	F	Α	V	v	K	K	s		L	140
141	Н	W	С	N	N	V	P	D	I	F	Ι	I	N	L	s	v	v	D D	_	L	160
161	F	L	L	G	М	Ρ	F	М	Ι	_H	Q	L	М	G	N	G	V	W	Н	F	180
181	G	E		М	С	Т	L	I	Т	A	M	D	A	N	S	0	F	Т	s	T	200
201	<u>Y</u>	II	_	Т	A	М	Α	I	D	R	Y	L	Α	Т	V	Н	P	I	s	s	220
221	Т	K	F	R	K	P	s	<u>V</u>	Α		L	V	Ι	С	L	L	W	Α	L	s	240
241	F	I.	s	I	T	Р	V	W	L	-		R	L	Ι	Ρ	F	Р	G	G	Α	260
261	<u>v</u> _	G	.C	G	Ι	R	L	P	N	P	D	Т	D	L	Y	W	F	Т	L	Y	280
281	0	F	F	L	Α	F	Α	•	P	F	V	V	I	Т	A	Α	Y	V	R	I	300
301	L	Q	R	M	Т	s	s	V	Α	P	Α	s	Q	R	S		R	L	R	Т	320
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# IDORGELY IDEOUS

# FIGURE 4

,	GCAGGCGACCTGCACCGGCTGCATGGATCTGCAAACCTCGTTGCTGTCCACTGGCCCCAA	09
61	TGCCAGCAACATCTCCGATGGCCAGGATAATCTCACATTGCCGGGGTCACCTCCTCGCAC	120
21	AGGGAGTGTCTCCTACATCAACATCATTATGCCTTCCGTGTTTGGTACCATCTGTCTCCT	180
81	GGGCATCGTGGGAAACTCCACGGTCATCTTTGCTGTGGAGAAGAAGTCCAAGCTACACTG	240
41	GTGCAGCAACGTCCCCGACATCTTCATCATCACCTCTCTGTGGTGGATCTGCTCTTCCT	300
0.1	GCTGGGCATGCCTTTCATGATCCACCAGCTCATGGGGAACGGCGTCTGGCACTTTGGGGA	360
19	AACCATGTGCACCCTCATCACAGCCATGGACGCCAACAGTCAGT	420
21	CCTGACTGCCATGACCATTGACCGCTACTTGGCCACCGTCCACCCATCTCCTCCACCAA	480
81	GTTCCGGAAGCCCTCCATGGCCACCCTGGTGATCTGCCTCCTGTGGGCGCTCTCCTTCAT	540
41	CAGTATCACCCCTGTGTGGCTCTACGCCAGGCTCATTCCCTTCCCAGGGGGTGCTGTGGG	009
01	CTGTGGCATCCGCCTGCCAAACCCGGACACTGACCTCTACTGGTTCACTGTACCAGTT	099
199	TITCCTGGCCTTTGCCCTTCCGTTTGTGGTCATTACCGCCGCATACGTGAAAATACTACA	720
21	GCGCATGACGTCTTCGGTGGCCCCCAGCCTCCCAACGCAGCATCCGGCTTCGGACAAAGAG	780
81	GGTGACCCGCACGGCCATTGCCATCTGTCTGTCTTTTTGTGTGTG	840
41	TGTGCTGCAGCTGACCCAGCTGTCCATCAGCCGCCCGACCCTCACGTTTGTCTACTTGTA	006
01	CAACGCGCCCATCAGCTTGGCTATGCTAACAGCTGCCTGAACCCCTTTGTGTACATAGT	096
191	GCTCTGTGAGACCTTTCGAAAACGCTTGGTGTTGTCAGTGAAGCCTGCAGCCCAGGGGCA	1020
121	GCTCCGCACGGTCAGCAACGCTCAGACAGCTGATGAGGAGAGGACAGAAAGCAAAGGCAC	1080
181	CIGACAATTCCCCAGTCGCCTCCAAGTCAGGCCACCCCATCAAACCGTGGGGAGAGATAC	1140
41	TGAGATTAAACCCAAGGCTACCCTGGGAGAATGCAGAGGCTGGAGGCTGGGGGGCTTGTAG	1200
5	CAACCACATTCCAC	1214

# FIGURE 5

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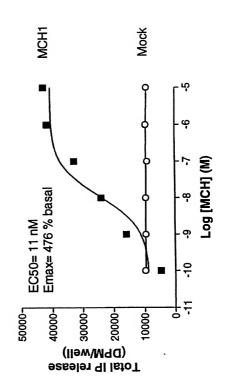
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HUHKIHKKITKKA>>KK
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O R K S H P F P K H B B H P C H O B
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FIGURE 6

IP release in MCH1- and mock-transfected Cos-7 cells



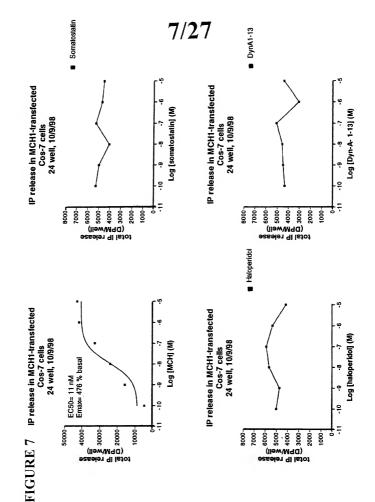
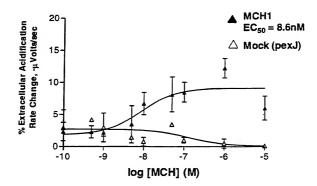


FIGURE 8 8/27
Microphysiometer Response CHO cells



# Microphysiometer Response CHO cells

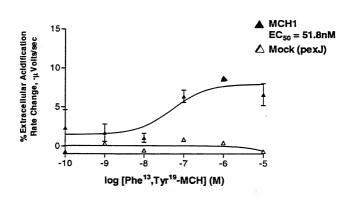
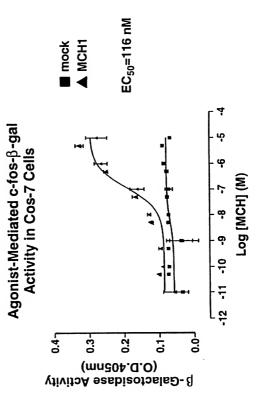
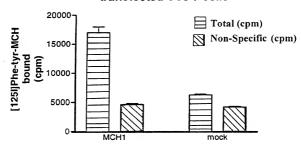


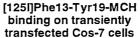
FIGURE 9

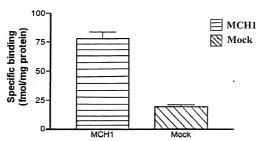


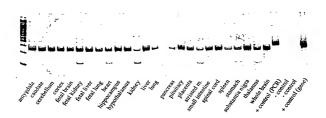
#### FIGURE 10

[125I]Phe13-Tyr19-MCH binding on transiently transfected Cos-7 cells









40 GCQATEEDPL PDCGACAPGQ GCQATEEDPL PDCGACAPGQ GCQATEEDPL PDCGACAPGQ	80 WEQATGTGWM DLEASLLPTG WEQATGTGWM DLEASLLPTG WEQATGTGWM DLEASLLPTG
GCQATEEDPL	WEQATGTGWM
GCQATEEDPL	WEQATGTGWA
GCQATEEDPL	WEQATGTGWA
GRAVGLGGGS	AWVEGSSARL
GRAVGLGGGS	AWVEGSSARL
GRAVGLGGGS	AWVEGSSARL
MSVGAMKKGV MSVGAMKKGV MSVGAAKKGV	41 GGRRWRLPQP GGRRWRLPQP GGRRWRLPQP
TL231	TL231
R106	R106
R114	R114
B0120	B0120

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10	10	PNASNTSDGP	PNASNTSDGP	PNASNTSDGP	PNASNTSDGP
		TL231	R106	R114	B0120

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FIGURE 16

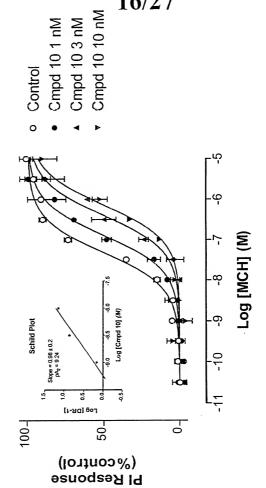
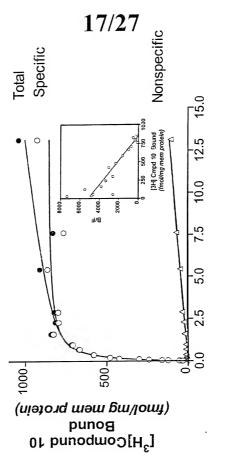
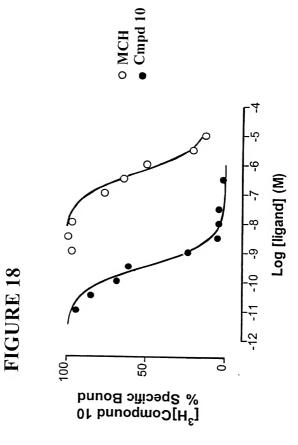


FIGURE 17



[<sup>3</sup>H]Compound 10 Free (*nM*)



#### FIGURE 19

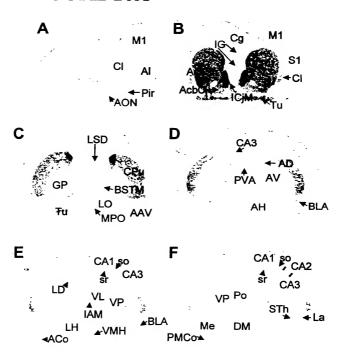
# Total MCH1 Receptor Binding



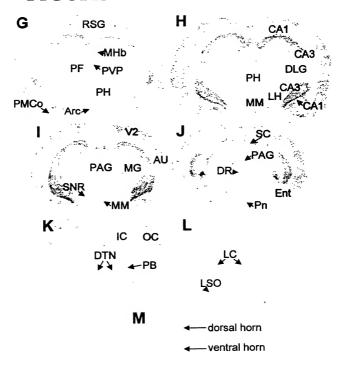
Nonspecific binding

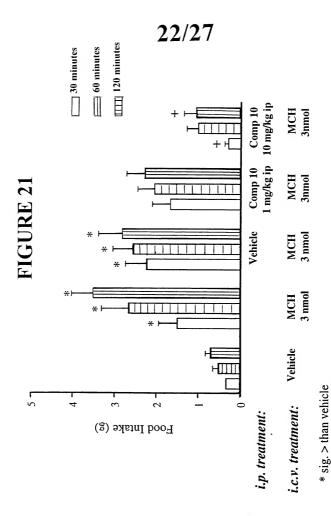
В

#### FIGURE 20A

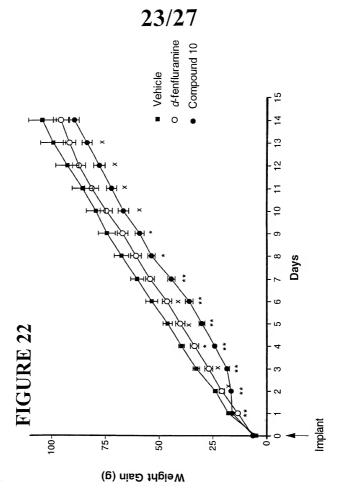


## FIGURE 20B





+ sig. < than veh+MCH



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